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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,436	08/21/2003	Martin Gleave	UBC.P-030	9171

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,436	GLEAVE ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4, 10-14, drawn to a RNA molecule targeted to a gene encoding clusterin, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

II. Claims 1-3, 5, 10-13 and 15, drawn to a RNA molecule targeted to a gene encoding IGFBP-5, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

III. Claims 1-3, 6, 10-13 and 16, drawn to a RNA molecule targeted to a gene encoding IGFBP-2, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

IV. Claims 1-3, 7, 10-13 and 17, drawn to a RNA molecule targeted to genes encoding IGFBP-2 and IGFBP-5, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

V. Claims 1-3, 8, 10-13 and 18, drawn to a RNA molecule targeted to a gene encoding MITF, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

VI. Claims 1-3, 9, 10-13 and 19, drawn to a RNA molecule targeted to a gene encoding B-raf, classifiable in class 536, subclass 24.5. This group is subject to an additional restriction.

VII. Claims 20-23 and 29, drawn to a method of treating cancer that expresses clusterin by administering an RNA molecule targeted to clusterin, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

VIII. Claims 20-22, 24 and 29, drawn to a method of treating cancer that expresses IGFBP-5 by administering an RNA molecule targeted to IGFBP-5, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

IX. Claims 20-22, 25 and 29 drawn to a method of treating cancer that expresses IGFBP-2 by administering an RNA molecule targeted to IGFBP-2, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

X. Claims 20-22, 26 and 29 drawn to a method of treating cancer that expresses IGFBP-2 and IGFBP-5 by administering an RNA molecule targeted to IGFBP-2 and IGFBP-5, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

XI. Claims 20-22, 27 and 29 drawn to a method of treating cancer that expresses MITF by administering an RNA molecule targeted to MITF, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

XII. Claims 20-22, 28 and 29 drawn to a method of treating cancer that expresses B-raf by administering an RNA molecule targeted to B-raf, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

XIII. Claim 30, drawn to a method of treating Alzheimer by administering an RNA molecule, classifiable in class 514, subclass 44. This group is subject to an additional restriction.

The inventions are distinct, each from the other because of the following reasons:

Inventions of group I, II, III, IV, V and VI, are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the RNA molecules of groups I-VI are materially different because they each have a different structure and they each target different transcriptional genes in cancers and regulate expression of different target genes (see Tables 1-6). Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group I can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding clusterin of group VII. Furthermore restriction is

proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating cancer that expressed IGFBP-5, as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating cancer that expressed IGFBP-2, as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for

one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group I and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating cancer that expressed IGFBP-2 and IGFBP-5, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group I and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating cancer that expressed MITF, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating cancer that expressed B-raf, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group I and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group I is a compound inhibitor of a gene expression clusterin, which is materially different than a method of treating Alzheimer by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5, which is materially different than a method of treating cancer that expressed clusterin, as present in group VII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group II can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding IGFBP-5 of group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5 which is materially different than a method of treating cancer that expressed IGFBP-2, as present in group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5, which is materially different than a method of treating cancer that expresses IGFBP-2 and IGFBP-5, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group II and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have

materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5, which is materially different than a method of treating cancer that expresses MITF, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group II and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5, which is materially different than a method of treating cancer that expresses B-raf, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group II is a compound inhibitor of a gene expression IGFBP-5, which is materially different

than a method of treating Alzheimer by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2, which is materially different than a method of treating cancer that expresses clusterin, as present in group VII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2, which is materially different than a method of treating cancer that expresses IGFBP-5 as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for

one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group III and group IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group III can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding IGFBP-2 of group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2 which is materially different than a method of treating cancer that expressed IGFBP-2 and IGFBP-5, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group II and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2, which is materially different than a method of treating cancer that expresses MITF, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2, which is materially different than a method of treating cancer that expresses B-raf, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group III and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expression IGFBP-2, which is not used in a method of treating Alzheimer's disease by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group III is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not used in a method of treating cancer that expresses clusterin, as present in group VII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have

materially different modes of operation with different effects. For example, the compound of group IV is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not necessarily used in a method of treating cancer by administration of a RNA molecule targeted only to IGFBP-5, as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group IV and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group IV is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not necessarily used the method of treating cancer by administration of a RNA molecule targeted only to IGFBP-2, as present in group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group IV can be used as a probe in *in situ* hybridization, which is materially different than the methods of

inhibiting expression of a gene encoding IGFBP-5 and IGFBP-2 as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group IV is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not used in a method of treating cancer that expresses MITF, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group IV is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not used in a method of treating cancer that expresses B-raf, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for

one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group IV is a compound inhibitor of a gene expressing IGFBP-2 and IGFB-5, which is not used in a method of treating Alzheimer's disease by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not used in a method of treating cancer that expresses clusterin, as present in group VII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not used in a method of treating cancer by administration of a RNA molecule targeted to IGFBP-5, as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group V and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not necessarily used the method of treating cancer by administration of a RNA molecule targeted only to IGFBP-2, as present in group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group IV and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not used in a method of treating cancer that expresses IGFBP-2 and IGFBP-5, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group V can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding MITF as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have

materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not used in a method of treating cancer that expresses B-raf, as present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group V and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group V is a compound inhibitor of a gene expressing MITF, which is not used in a method of treating Alzheimer's disease by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of

group VI is a compound inhibitor of a gene expressing B-raf, which is not used in a method of treating cancer that expresses clusterin, as present in group VII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group VI is a compound inhibitor of a gene expressing B-raf, which is not used in a method of treating cancer by administration of a RNA molecule targeted to IGFBP-5, as present in group VIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application

Inventions of group VI and group IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group VI is a compound inhibitor of a gene expressing B-raf, which is not necessarily used the method of treating cancer by administration of a RNA molecule targeted only to IGFBP-2, as

present in group IX. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group VI is a compound inhibitor of a gene expressing B-raf, which is not used in a method of treating cancer that expresses IGFBP-2 and IGFBP-5, as present in group X. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group VI is a compound inhibitor of a gene expressing B-raf, which is not used in a method of treating cancer that expresses MITF, as present in group XI. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not

necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product RNA molecule of group VI can be used as a probe in *in situ* hybridization, which is materially different than the methods of inhibiting expression of a gene encoding B-rafas present in group XII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VI and group XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the compound of group VI is a compound inhibitor of a gene expressing B-raf, which is not used in a method of treating Alzheimer's disease by administration of a RNA molecule, as present in group XIII. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Inventions of group VII, VIII, IX, X, XI, XII and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different methods are not disclosed as useful together because they have materially different modes of operation with different effects. For example, the methods of treating cancer by administration of RNA molecules targeted to clusterin, IGFBP-5, IGFBP-2 and IGFBP-5 simultaneously, MITF or B-raf are all unrelated because each method is not disclosed as useful together and further each method is materially different because each RNA molecule targets different regions of different genes (see Tables 1-6) and regulate expression of different target genes (see Examples 20 and 21). Additionally, the above methods are materially different and than the method of treating an Alzheimer's disease by administration of a RNA molecule and not disclosed as capable of use together. Furthermore restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. It is therefore a burden to search these inventions in a single application.

Furthermore, should applicants elect to prosecute Group I, this Group is subject to further restriction as follows. Claim 4 is subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 – PRACTICE RE MARKUSH-TYPE CLAIMS – if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claims on the merits, even though

they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 300 (CCPA 1980); and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structure feature disclosed as being essential to that utility.

Claim 4 specifically claims RNA SEQ ID NOS as listed, which are targeted to and modulate the expression of clusterin. Although the RNA sequences claimed each target and modulate expression of clusterin, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of clusterin nucleic acid (see Table 1). As such the Markush/genus of RNA sequences in claim 4 is not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 4 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 4. Note that this is not a species election.

Furthermore, should applicants elect to prosecute Groups I-XIII, these Groups are subject to further restriction as follows. Claims 4-9, 14-19, 23-28 and 30 are subject to an additional restriction since they are not considered to be a proper genus/Markush. See MPEP 803.02 – PRACTICE RE MARKUSH-TYPE CLAIMS – if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 300 (CCPA 1980); and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structure feature disclosed as being essential to that utility.

Claims 4, 14, 23 and 30 specifically claim RNA SEQ ID NOS 1-16, 58, 59, 61, 62, 64, 65, 67 and 68, which are targeted to and modulate the expression of clusterin. Although the RNA sequences claimed each target and modulate expression of clusterin, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of

clusterin nucleic acid (see Table 1). As such the Markush/genus of RNA sequences in claims 4, 14 or 23 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 4, 14 or 23 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 4, 14 or 23. Note that this is not a species election.

Claims 5, 15 and 24 specifically claim RNA SEQ ID NOS 17-30, which are targeted to and modulate the expression of IGFBP-5. Although the RNA sequences claimed each target and modulate expression of IGFBP-5, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of IGFBP-5 nucleic acid (see Table 2). As such the Markush/genus of RNA sequences in claims 5, 15 or 24 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 5, 15 or 24 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 5, 15 or 24. Note that this is not a species election.

Claims 6, 16 and 25 specifically claim RNA SEQ ID NOS 31-38, which are targeted to and modulate the expression of IGFBP-2. Although the RNA sequences claimed each target and modulate expression of IGFBP-2, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of IGFBP-2 nucleic acid (see Table 3). As such the Markush/genus of RNA sequences in claims 6, 16 or 25 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 6, 16 or 25 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 6, 16 or 25. Note that this is not a species election.

Claims 7, 17 and 26 specifically claim RNA SEQ ID NOS 39-44, which are targeted to and modulate the expression of IGFBP-2 and IGFBP-5. Although the RNA sequences claimed each target and modulate expression of IGFBP-2 and IGFBP-5, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of IGFBP-2 and IGFBP-5 nucleic acid (see Table 4). As such the Markush/genus of RNA sequences in claims 7, 17 or 26 are not considered to constitute a proper genus, and are therefore subject to restriction.

Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 7, 17 or 26 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 7, 17 or 26. Note that this is not a species election.

Claims 8, 18 and 27 specifically claim RNA SEQ ID NOS 39-44, which are targeted to and modulate the expression of MITF. Although the RNA sequences claimed each target and modulate expression of MITF, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of MITF nucleic acid (see Table 5). As such the Markush/genus of RNA sequences in claims 8, 18 or 27 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 8, 18 or 27 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 8, 18 or 27. Note that this is not a species election.

Claims 9, 19 and 28 specifically claim RNA SEQ ID NOS 51-58, which are targeted to and modulate the expression of B-raf. Although the RNA sequences claimed each target and

modulate expression of B-raf, the instant RNA sequences are considered to be unrelated, since each RNA sequence claimed is structurally and functionally independent and distinct for the following reasons: each RNA sequence has a unique nucleotide sequence and each RNA sequence targets a different and specific region of B-raf nucleic acid (see Table 6). As such the Markush/genus of RNA sequences in claims 9, 19 or 28 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA sequences claimed in claims 9, 19 or 28 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA sequences. In view of the foregoing, one (1) RNA sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect a total of one (1) RNA sequence from claims 9, 19 or 28. Note that this is not a species election.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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Kimberly Chong
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